REMARKS

Enclosed please find Figure 1 consisting of 1 (one) sheet marked in red to identify the changes thereto. A discussion describing the revisions and the support therefore in the originally filed disclosure is provided below. Also enclosed please find Figure 1 consisting of 1 (one) sheet of the formal drawing for the subject application. In accordance with 37 C.F.R. 1.84(c), identifying indicia are provided on the backside of the sheet.

Applicants respectfully request that, prior to examination, Figure 1 be amended as shown on the marked-up version of Figure 1 and that pages 1 and 2 of the sequence listing be substituted with pages 1 and 2 submitted herewith. Applicants respectfully submit that no new matter is being added by the amendment of this figure and substitute sequence listing.

Figure 1 was originally filed with 9 (nine) residues inadvertently deleted from each row on the right hand side of the figure as indicated in the marked-up version submitted herewith. New Figure 1 sets forth the complete sequence for each organism. Applicants respectfully submit that, with the exception of the *Drosophila* ("fly") sequence, all the sequences in Figure 1 are known in the prior art, as described with genome database citations on page 3, lines 11-14 of the specification. Thus, one of ordinary skill in the pertinent art would have been able to obtain the correct sequences. In addition, the inadvertently omitted residues from the *Drosophila* sequence are described in the originally filed sequence listing in Sequence I.D No. 1. Thus, no new matter has been added by virtue of this amendment.

Applicants further request that pages 1 and 2 of the sequence listing be
replaced with the substituted pages submitted herewith. The Sequence I.D. No.1 in
the original sequence listing was filed with 1 residue (K) inadvertently omitted in the
second line of the listing (EIKSLED in the original should read EIK**K**SLED). This
portion of the sequence was given correctly in the second line of the *Drosophila* ("fly")
sequence in Figure 1 as originally filed and was also correctly shown in Figure 6B as
originally filed. In addition, Sequence I.D. No.2 in the original sequence listing shows
the DNA sequence encoding the correct protein, enabling one of ordinary skill in the
pertinent art to obtain the correct sequence. Therefore, Applicants respectfully
submit that no new matter is being added by the amendment of this sequence listing.

Should the Examiner wish to discuss the above amendment, the undersigned
attorney would appreciate the opportunity to do so.

Applicants believe that additional fees are not required for consideration of the

within Preliminary Amendment. However, if for any reason a fee is required, a fee paid

is inadequate or credit is owed for any excess fee paid, you are hereby authorized and

requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

Date: 5/2/01

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omitted in original (handwritten, top right)

Figure 1:   multiple sequence alignment

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yeast      MSTLIPPPSKKQKKEAQLPREVAIIPKDLPNVSIKFQALDTGDNVGGALRVPGAISEKQL
c.elegans  ------------------------------PQISVSEDENELG---GSGILVPVDISTNEL
fly        -------------------MQETDTEQEATPHTIQARLVYTGEEAGPPIDLPAGITTQQL
mouse      --------------------EEAAAGD-VQRLLVQFQDEGGQLLGSPFDVPVDITPDKL
human      ---------------------------------------GSPFDVPVDITPDRL
frog       --------------------MKEDVGRLLIQFKNENGEGLGTPFDVPLDITPDKL
                                              *   : :* *:  ..*

yeast      EELLNQLNGTSDDPVPYTFSCTIQGKKASDPVKTIDITDNLYSSLIKPGYNSTEDQITLL
c.elegans  QILCNQLLGSR---FCLNNEFSVSG---------AEIVDSIRKSLEEIDFET----LKLV
fly        GLICNALLKNE----EATPYLFFVGE-------DEIKKSLEDTLDLASVDT-ENVIDIV
mouse      XLVCNALL-AQEEPLPLAFYVHD----------AEIVSSLGKTLESQSV-ETEKIVDII
human      QLVCNALL-AQEDPCPLAFFVHD----------AEIVSSLGKTLESQAV-ETEKVLDIY
frog       QLVCNALL-QEEDPVPLAFFVQD----------LEIVTSLDKTLEKQSV-ETEKVIDII
                : * *                        :*   .:  .:*        : :

yeast      YTPRAVFKVKPVTRSSSAIAGHGSTILCSAFAPHTSSRMVTGAGDNTARIWDCDTQTPMH
c.elegans  YQPQAVFRVRPVTRCSASIPGHGEPVISAQFSPDGRG-LASGSGDQTMRIWDIELELPLH
fly        YQPQAVFKVRPVTRCTSSMPGHAEAVVSLNFSPDGAH-LASGSGDTTVRLWDLNTETPHF
mouse      YQPQAVFRVRAVTRCTSS-----------------------------------------
human      -QPQXLFRVRAVTRCTS------------------------------------------
frog       YQPQAVFKVRAVTRCTSSLEGHTEAVISVAFSPTGKY-LASGSGDTTVRFWDLSTETPHF
                *:  :*:*:.***.::

yeast      TLKGHYNWVLCVSWSPDGEVIATGSMDNTIRLWDPKSGQCLGDALRGHSKWITSLSWEPI
c.elegans  TCKSHKSWVLCIAWSPDATKIASACKNGEICIWNAKTGEQIGKTLKRHKQWIXXLAWQP-
fly        TCTGHKQWVLCVSWAPDGKRLASGCKAGSIIWDPETGQQKGRPLSGHKKHINCLAWEPY
mouse      -----------------------------------------------------------
human      -----------------------------------------------------------
frog       TSKGHTHWVLSIAWSPDGKKLASGCKNSQIFIWDPSTGKQIGKPLTGHSKWITWLCWEPL

yeast      LVKPGSKPRLASSSKDGTIKIWDTVSRVCQYTMSGHTNSVSCVKWGGQGLLYSGSHDRTV
c.elegans  -------------------TVKMWR-----------ADDGVMCRNMTG----------
fly        HRDPECR-KLASASGDGDCRIWDVKLGQCLMNIAGHTNAVTAVRWGGAGLIYTSSKDRTV
mouse      -----------------------------------------------------------
human      -----------------------------------------------------------
frog       HLNPESRY-LASASKDCTIRIWDTVMGQCQKILTSHTQSVTAVKWGGDGLLYSSSQDRTI

yeast      RVWDINSQGRCINILKSHAHWVNHLSLSTDYALRIGAFDHTGKK-----PSTPEEAQKKA
c.elegans  ----------------HAHWINTLALNTDYALRTSCFE---------PSK-------
fly        KMWR-AADGILCRTFSGHAHWVNNIALSTDYVLRTGPFHPVKDRSKSHLSLSTEELQESA
mouse      -----------------------------------------------------------
human      -----------------------------------------------------------
frog       KAWR-AQDGVLCRTLQGHAHWVNTMALSTDYVLRKGAFNPADAS--VNPQDMSGSLEVLK

yeast      LENYEKICKKNGNSEEMMVTASDDYTMFLWNPLKSTKPIARMTGHQKLVNHVAFSPDGRY
c.elegans  ---------------------------------------INRMTGHMQLVNQVVFSPDTRY
fly        LKRYQAVCP---DEVESLVSCSDDNTLYLWRN-NQNKCVERMTGHQNVVNDVKYSPDVKL
mouse      -----------------------------------------------------------
human      -----------------------------------------------------------
frog       EKALKRSNEVRGQGPERLVSGSEDFTLFLWAPAEEKKPLQRMTGHQALINEVLFSPDTRI

yeast      IVSASFDNSIKLWDGRDGKFISTFRGHIASVYQVAWSSDCRLLVSCSKDTTLKVWDVRTR
c.elegans  IASASFDKSVKLWCGRTGKYLASFRGHVGPVYQVAWSADSRLLVSGSADSTLKVFELKTK
fly        IASASFDKSVRLWRASDGQYMATFRGHVQAVYTVAWSADSRLIVSGSKDSTLKVWSVQTK
mouse      -----------------------------------------------------------
human      -----------------------------------------------------------
frog       IASASFDKSIKLWDGKTGKFLTSLRGHVSAVYQIAWSADSRLLVSGSSDSTLKVWDSKTK

yeast      KLSVDLPGIKTKLY-VDWSVDGKRVCSGGKDKMVRLWTH
c.elegans  SLYYDLPGHGDEVFTVDWSPEGTKVVSGGKDKVLKLW--
fly        KLAQELPGHADEVFGVDWAPDGSRVASGGKDKVIKLWAY
mouse      ---------------------------------------
human      ---------------------------------------
frog       KLLIDLPGHADEVYSVDWSPDGQRVASGGKDKCLRIWRK
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Omitted in original (handwritten, bottom right)

Sequence I.D. No.1: Drosophila Notchless protein

MQETDTEQEATPHTIQARLVYTGEEAGPPIDLPAGITTQQLGLICNALLKNEEA
TPYLFFVGEDEIKKSLEDTLDLASVDTENVIDIVYQPQAVFKVRPVTRCTSSMP
5 GHAEAVVSLNFSPDGAHLASGSGDTTVRLWDLNTETPHFTCTGHKQWVLCV
SWAPDGKRLASGCKAGSIIIWDPETGQQKGRPLSGHKKHINCLAWEPYHRDP
ECRKLASASGDGDCRIWDVKLGQCLMNIAGHTNAVTAVRWGGAGLIYTSSK
DRTVKMWRAADGILCRTFSGHAHWVNNIALSTDYVLRTGPFHPVKDRSKSH
LSLSTEELQESALKRYQAVCPDEVESLVSCSDDNTLYLWRNNQNKCVERMT
10 GHQNVVNDVKYSPDVKLIASASFDKSVRLWRASDGQYMATFRGHVQAVYT
VAWSADSRLIVSGSKDSTLKVWSVQTKKLAQELPGHADEVFGVDWAPDGSR
VASGGKDKVIKLWAY

Sequence I.D. No. 2: Drosophila *Nle* cDNA
15

aattcccaaaaaATGCAGGAGACGGACACGGAGCAAGAGGCCACGCCACATACG
ATACAGGCGCGCCTCGTTTACACGGGCGAGGAAGCCGGCCCGCCAATCGA
CCTGCCGGCAGGAATCACTACCCAGCAATTGGGACTGATTTGCAACGCGC
TGCTGAAAAACGAGGAAGCCACTCCATATTTGTTTTTCGTGGGCGAGGAT
20 GAGATCAAGAAGAGCCTGGAGGACACGTTGGACTTGGCGTCAGTGGACA
CCGAAAACGTGATCGATATTGTGTATCAGCCACAGGCGGTTTTCAAAGTG
CGCCCAGTGACAAGATGCACGAGTTCCATGCCGGGACACGCCGAGGCTGT
GGTTTCGCTGAATTTCAGCCCGGATGGTGCTCATCTCGCCAGTGGAAGTG
GCGACACCACAGTGCGATTGTGGGATCTTAACACAGAGACACCGCACTTC
25 ACCTGCACAGGTCATAAGCAGTGGGTTCTGTGCGTATCCTGGGCTCCGGA
TGGCAAACGGTTGGCCAGCGGTTGCAAAGCGGGCTCTATAATCATCTGGG
ACCCGGAGACGGGTCAGCAGAAGGGGCGACCCTTGAGTGGGCACAAGAA
ACACATCAACTGCCTCGCCTGGGAACCGTATCATCGCGATCCGGAGTGCA
GGAAACTTGCTTCCGCCAGTGGAGACGGGGACTGCCGGATTTGGGACGTA
30 AAATTGGGCCAGTGCCTTATGAACATTGCCGGACACACAAATGCTGTGAC
AGCAGTGAGATGGGGTGGAGCGGGCCTTATTTATACATCCTCCAAAGATC
GCACAGTGAAGATGTGGCGAGCAGCTGATGGAATCTTGTGCCGGACGTTC
TCTGGCCAAGCTCACTGGGTAAACAACATTGCGCTGAGCACCGATTACGT
CCTGCGCACTGGTCCATTCCATCCGGTGAAGGATCGCTCCAAGAGCCACC

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TCAGTTTGAGCACTGAGGAATTGCAGGAATCTGCCTTGAAGCGCTACCAG
GCCGTGTGCCCTGACGAGGTGGAGTCGCTGGTTTCCTGTTCGGATGACAA
CACCCTCTATCTGTGGCGGAACAACCAGAACAAGTGCGTTGAGCGCATGA
CAGGGCACCAGAACGTGGTCAACGATGTGAAATATTCGCCGGATGTAAAG
5   CTAATTGCGTCTGCTTCATTTGACAAGTCAGTGCGTCTGTGGCGAGCCAGC
GATGGTCAGTACATGGCCACCTTCCGGGGGTCATGTGCAGGCTGTTTACAC
GGTTGCCTGGTCCGCGGACTCCCGCTTGATTGTTTCCGGCAGCAAAGACTC
AACTCTAAAAGTATGGAGTGTGCAGACGAAGAAACTGGCACAGGAGCTG
CCTGGACATGCGGATGAGGTGTTCGGAGTGGACTGGGCGCCCGATGGCTC
10   TAGAGTTGCCTCTGGTGGCAAGGACAAAGTTATAAAGCTATGGGCTTATT

AAcaaatcattaacttgtacacggtaagaaaatacttaggaataaagtaaaacgtcctgagtaaaaaaaaaaaaaaaaaaa
aaaaaaaaaaaaaaaaaaaaa